Understanding the Drivers of Value Creation for Biopharmaceuticals around the Time of Drug Launch

by

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Submitted to the Harvard-MIT Division of Health Sciences and Technology on May 21, 2012 in Partial Fulfillment for the Degree of Master of Science in Health Sciences and Technology at the Massachusetts Institute of Technology

Abstract

The purpose of this research is to investigate potential strategic variables that executives at small to mid-sized biopharmaceutical companies should consider during the period of a drug launch. Bringing a product to market is a critical event for any biopharmaceutical company. It marks a major turning point within the biopharmaceutical's lifecycle and the company that can successfully launch a product will be viewed as a different asset class. Therefore, it is critical to understand potential drivers of the value and to encourage executives to raise probing questions when they are considering the next round of financing or whether to provide guidance.

This study analyzed forty-six non-generic, therapeutic drugs launched in the US during January 2000- December 2009 by small to mid-sized biopharmaceutical companies with market capitalizations less than $20 billion at the time of launch. Predictor variables that were initially considered in the analysis are the following: management providing a sales guidance (binary), partnership (binary), market size of the partner(s) at the time of launch, specialty/primary care indication (binary), difference between year two actual sales number and that of pre-launch estimate, difference between year two actual sales number and that of post-launch estimate, financing activity prior to launch (binary), financing activity after launch (binary), average pre-launch file-to-offer discount, average post-launch file-to-offer discount, number of drugs launched by the same company (control variable) and NBI performance (control variable).

Multiple linear regression analyses were then performed to determine which of these parameters were predictive of changes in stock price and changes in market capitalization. Those companies that did not provide guidance at the time of launch and raised additional capital within two years after launch performed better than those that did otherwise. Neither a partnership nor the market size of the partner contributed to either of the outcome measures. Whether or not the product is a specialty product also did not make any significant contribution to the models.

The results from this study suggest several possible strategic and actionable items that can guide management to ask the right questions during the period around a drug launch.

Thesis Supervisor: Brian Pereira, MD, MBA

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Dedication

To my parents, Hea Young and Ki Jo, for their unconditional love and for providing me with endless opportunities and support in every endeavor I undertook

To my sister and my best friend, Jung Min, for always being there as my biggest confidant

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1. Introduction

1.1 Background

Executives at growing biopharmaceutical companies are faced with numerous challenges. Companies not only have to exquisitely manage the commercialization of their products but also have to develop a deep enough pipeline. In addition, there are inherent risks that are associated with commercializing a product, such as uncertainty associated with the reimbursement landscape and the performance of the product in its therapeutic area, to name a few.

Drug commercialization is one of the most critical events for biopharmaceutical companies. The drug launch can serve as a significant value inflection point for a company given high investor interest at this juncture, and is often subject to a high degree of investor speculation. In addition, launching a drug is costly and often requires the company to seek additional sources of capital to continue its progress.

Given the importance of a drug launch to a company's life cycle, our research sets out to identify potential drivers that may play a meaningful role in a successful drug launch and thereby to encourage the management to ask probing questions as they are about to launch a drug. The study has found an interesting set of observations from a ten-year period of 46 product launches by publicly traded small- to mid-sized biopharmaceutical companies.

1.2 Defining the biopharmaceutical industry

There are many definitions of "biopharmaceuticals" not only within the scientific community but also in other industry sectors and the press (Rader 2005). Classifying companies as biopharmaceutical can be even more confusing. Some biopharmaceutical companies, such as Biogen, Amgen and Genzyme, develop, manufacture, and market synthetic drugs. Conversely, traditional large pharmaceutical companies, including Hoffmann-La Roche and Merck, are also involved in biopharmaceuticals. Even though the term "biopharmaceutical" (or "biotechnology")

company usually refers to a firm whose goal is to develop new protein-based molecules, this study will use the broader definition to include those firms developing any new drug, be it a biologic or small molecule.

1.2.1 Business dynamics within the sector

Overall, the introduction of biotechnology added complexity to drug development. In the late 1990s and into early 2000, biotechnology matured relatively rapidly as it underwent a boom. The initial public offering (IPO) served as a reasonable exit option for early stage biotech investors to achieve a satisfying return on their investments. In addition, public and private investors provided sources of capital to fund innovation to reach a value inflection point.

Today, the health care industry as a whole is undergoing a major transformation into an outcomes-driven ecosystem. This shift is driven largely by the need to make the health care sustainable with its cost outpacing inflation and fiscally constrained budgets. Growing costs are at odds with legislative efforts to expand access to greater portions of the population, so payers will inevitably focus more on the cost-effectiveness of a medical intervention. Drug companies will face increased pressure on prices and demand to prove the comparative effectiveness and efficiency of their products. Ever changing FDA regulatory requirements increase uncertainty and risks associated with drug development. All of this points to an extremely challenging environment where biotechnology companies will need to spend more time and financial resources on additional data (Ernst & Young 2011).

1.2.2 Drug development and cost

It is costly to discover and develop a new drug due to expensive research processes, costs associated with clinical trials, regulatory approval procedures and costs associated with manufacturing. A study by DiMasi et al. estimates the average capitalized cost per approved biopharmaceutical in 2006 to be approximately $1.24B. In addition, the authors found that this cost along with the time it takes to bring a new drug to market have increased significantly over the last 10 years (DiMasi and Grabowski 2007). Not surprisingly such increased cost associated with R&D has translated to increased need for funding.

In addition to the high cost associated with drug development, there is an extremely high risk of failure in biopharmaceutical research and development. According to a recent report from KMR Group, a biopharmaceutical industry consultancy, the average success rate from preclinical to clinical studies for biologics was approximately 12% and that of small molecule drugs was about 2%. The biologics success rates for each clinical hurdle are the following: 17% at Phase I, 27% at Phase II, 58% at Phase III and 82% at the registration phase. For small molecules the success was calculated to be 4%, 9%, 44% and 78%, respectively (Philippidis 2012). The Tufts Center for the Study of Drug Development has shown that when looking beyond success in clinical studies, large molecules had a clinical approval success rate of 32% whereas small molecules had a rate of 13% for the period between 1993 and 2004 (Figure 1, DiMasi et al. 2010).

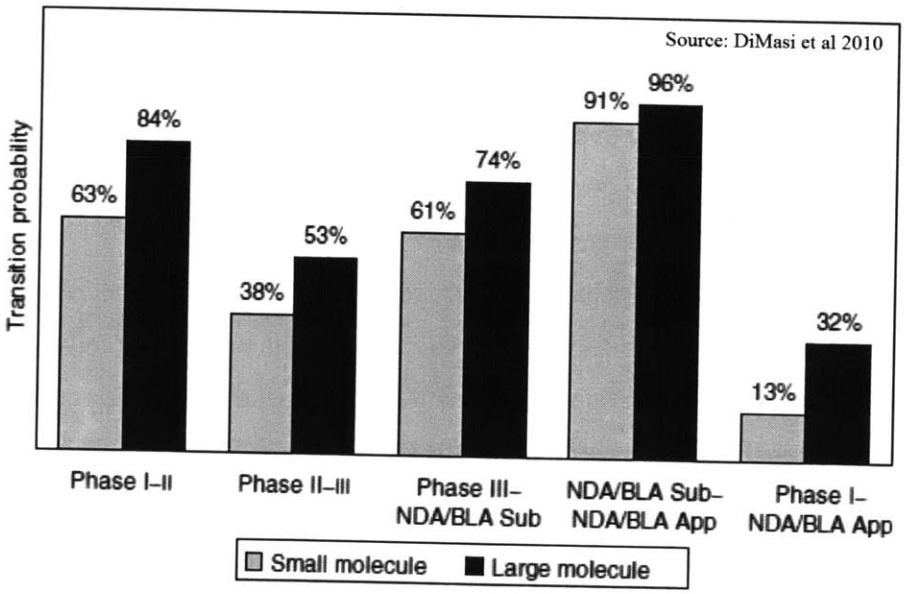
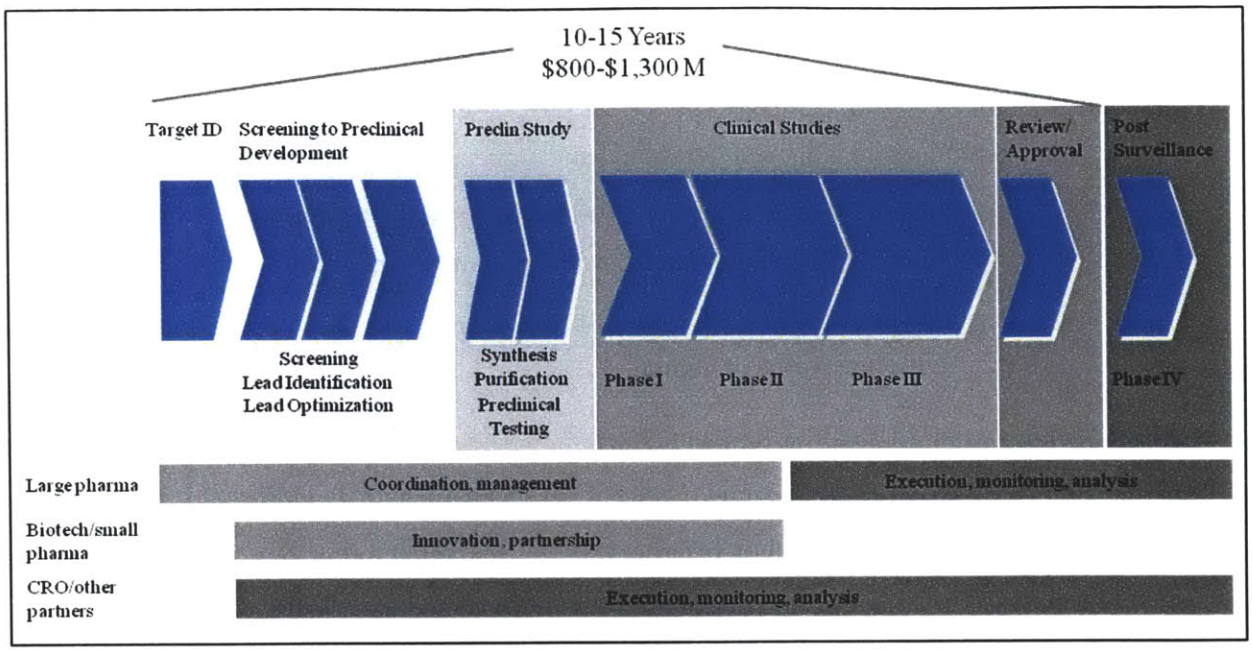


Figure 1 Phase transition probabilities and clinical approval success rates for small and large molecules

Lastly, drug development requires many years. A typical timeframe can take up to 10-15 years from the discovery of the molecule in a laboratory to its marketing stage (Figure 2). Given that most patents expire after 20 years, such a long development timeframe for typical biopharmaceutical molecules would only leave behind a very short window of 5-10 years to generate market revenue.



Source: Modified Kaitlin 2010; 15.363 Lecture Fleming J., Zarur A., MIT Sloan School of Management Feb 2010

Figure 2 Typical phases from research to post-market for a drug candidate and integrated R&D roles of major stakeholders

The relationship between the biopharmaceutical industry and the traditional pharmaceutical sector is a rather interesting one. Biopharmaceutical companies tend to have limited resources and may gain access to capital by selling or out-licensing drug candidates or establishing alliances with pharmaceutical companies. On the other hand, pharmaceutical companies with a dried out drug pipeline seek out potential drug candidates being developed by the biopharmaceutical companies to fill their own pipelines.

1.3 The capital base available for the biopharmaceutical sector

1.3.1 Overview of the finance industry

This section will provide a broad overview of the relationship among the various players in the financial system. Simply a corporation can be viewed as an entity that raises capital and then puts that capital to work at whatever it is that company specializes in.

A corporation finances its activities by issuing equity via initial public offering (IPO) or secondary offering, issuing debt, and using cash flows from operations. The decisions about how much capital is required to achieve operational and strategic objectives will determine whether and in what proportion debt and equity will need to be raised. Companies make these decisions internally and sometimes will seek advice from investment banks.

1.3.2 Different forms of capital

As alluded to earlier, biopharmaceutical companies can obtain additional capital through partnerships with larger pharmaceutical companies. There are however other sources of capital such as venture capital, initial public offerings (IPOs), marketed follow ons, private investments in public equity (PIPE), registered direct offerings (RDOs) and bank loans.

Source of Capital	Typical Funding Structure
Venture Capital	Equity Investment Venture Debt
Private Equity	Equity Investment Project Financing Milestone Monetization
Investment Bank	IPO Marketed Follow On PIPE / RDO
Leveraged Recap	Convertible Debt
Corporate Partnership	Pharma In-house VC arms Equity Investment In-Licensing/Co-Development

Figure 3 Different types of capital sources for biopharmaceutical companies

The composition of capital sources for biopharmaceutical companies tends to vary with the different stages of the companies' life cycle, which will be discussed in Section 1.3.4. Overall, venture capital provides a large portion of funding for biopharmaceutical drug developing companies. Grants and loans are an important financial source in the early stages of drug

development, while IPOs and other types of public funding are mostly relevant in the later stages and for product candidates that are close to the market.

The global financial crisis in late 2008 had a wide-reaching impact on the economy as a whole, including biopharmaceutical companies. Their typical sources of capital adapted their investment strategies to respond to the new economic realities.

Venture Capital

Venture capital (VC) has always been based on three key elements: deal sourcing, monitoring and exiting. With a number of notable shifts in the investment landscape, many VC firms are shifting in what they invest in and their investment structures to increase capital efficiency and shorter development cycles.

For early stage companies, many VC firms are deploying portions of capital over time at several milestone-driven "tranches." Such structure seems to align incentives of VCs and those of companies. VCs can manage total return on investment as they can pull capital from their investors in a more staged manner and company management is driven to achieve upcoming milestones and stay focused throughout to deliver results.

With IPOs still being a challenging exit option, VC firms work towards increasing the likelihood of an exit by acquisition. New investments increase their focus on companies that develop products targeting diseases that fall within the portfolio strategy of established biopharmaceutical companies. VC firms therefore work with pharma earlier on in a company's life cycle and even form a partnership to receive guidance on how to design critical development stage studies (Licking 2009).

Private Equity

Non-venture capital private equity (PE) firms typically invest in mid-stage biotech companies using specific financing structures. There are two major forms of financing.

a. Project Financing

Project financing provides a unique source of non-dilutive capital for mid-stage biotech companies. Typically, a PE firm purchases the rights to one or more drug candidates in phase I development from a biotech company, forms a joint venture company around the assets and then hires the biotech company to conduct the phase II studies with varying degrees of external assistance such as contract research organizations. Upon successful completion of phase II trials, the biotech company then has the option to re-acquire the candidates at a pre-determined internal rate of return (IRR). The rationale behind this structure is that by taking the product to proof of concept in a quick and cost-efficient manner, the joint venture has now reached a major value inflection for the biotech company to raise additional capital on the public markets (Longman 2005).

b. Revenue Interest Financing

For companies with highly promising marketed products or drugs in post phase III, revenue interest financing allows them to raise relatively inexpensive, non-dilutive capital. Requiring fewer covenants than a traditional debt, such form of financing will also allow more flexibility for the company. In a typical revenue financing deal, the biotech company will receive an upfront payment in exchange for a percentage of the future royalty payments or of the future product revenue for a defined period of time (Levine 2008). If done right, a company could use a noncore asset to fund a promising product in the pipeline without partnering and independent of market conditions and potentially realize a greater value from the asset.

Investment Bank

Healthcare investment banks offer a variety of services to biotech companies including advising on M&A activity, IPOs, follow-on offerings, PIPEs, RDOs and private placements. An interesting trend in healthcare investment banking is its shift into the most specialized investment structures such as revenue interest financing which has been more typical for PE firms.

Corporate Partnership

Established biopharma companies with large amounts of cash yet dried out pipelines have taken a greater role in the financing of the biotech companies through their own corporate venture capital (CVC) investment and acquisition activities.

CVC arms have been around since the late 1970s but there has been an increased number of them including Genentech in 2002, Biogen Idec in 2004 and Boehringer Ingelheim in 2010 to name a few. There has been an increase in the number of deals done by these groups.

There has been a shift in the deal structure in acquisitions where pharma companies are looking for creative ways to share risks such as including contingent value rights (CVRs) or structuring deals based on options. Their structures are largely similar in that they allow risk sharing and bringing the valuations closer, but they differ in relative emphasis. Under CVR, a large portion of the purchase price will be paid only upon achieving predefined milestone events. CVRs have bigger up-front investment compared to option-based deals where the split may be closer to 50/50. In option-based transactions, an established biopharma will pay for the option to acquire a program or company after a specified milestone. Such structure allows both parties to share the development risk and bridge potential valuation gaps (Ernst & Young 2011).

In addition to pursuing acquisitions, an established biopharma company forms a strategic alliance with a biopharmaceutical company. In a strategic alliance, a biopharmaceutical company, the holder of an intellectual property (IP), partners with a larger pharmaceutical company for the development and exploitation of the IP.

Forming an alliance is different from licensing. Licensing typically refers to a passive relationship where the licensor is not required to do anything else but it passively collects royalties and other forms of milestone payments that are decided at the time of a license agreement. Strategic alliances on the other hand, involve more active relationships where both parties that are involved contribute different yet complementary capabilities. There are many types of strategic alliances but broadly speaking, there are two major types of alliances in the biopharmaceutical sector: co-development and co-marketing.

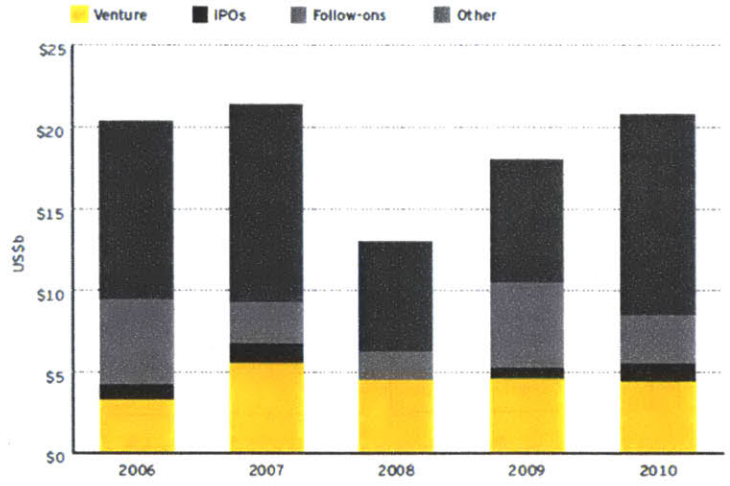
In a co-development alliance, an IP is typically licensed by a biopharma company to its partnering pharma, and both companies together jointly undertake the further development of a drug candidate from that IP. Developing a new IP that is based on the licensed IP is the aim of the collaboration. There are many different ownership structures for this newly developed IP. Overall, co-development alliance allows the biopharma to add value beyond just granting a license and therefore be entitled to a larger portion of payments than would otherwise.

In a co-marketing alliance, an IP is similarly licensed by a biopharma to its partner, but in addition, the partners together access their respective marketing networks and resources to jointly take the drug product to market (Mendes 2005).

1.3.3 Capital supply and financing gaps

According to a report by Ernst & Young, biotechnology companies across the US, Europe and Canada raised $ 25 billion in 2010, a number that's comparable to the amounts raised in the "easy money" years preceding the financial crisis of 2008. Such rebound is definitely impressive, but a careful analysis reveals that most of this capital belonged to small portion of the industry. The top 20% of US companies that were most successful in raising funds were responsible for 82.6% of capital; conversely those in the bottom 20% raised only 0.4% of funds in 2010.

The "Other" source of financing shown in Figure 4 includes $3.7 billion and $9.4 billion in 2009 and 2010, respectively, of debt raised by profitable companies in the US. Taking these amounts out from the sum, "innovation capital" raised by pre-commercial companies actually declined by 21% in 2010 (Ernst & Young 2011).



	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
IPOs	1,097	697	6	1,238	944	626	1,618	448	456	208	4,997
Follow-ons	2,971	5,165	1,715	2,494	5,114	3,952	2,846	2,825	838	1,695	14,964
Other	12,242	7,617	6,832	12,195	10,953	6,788	8,964	8,306	5,242	3,635	9,987
Venture	4,409	4,556	4,445	5,464	3,302	3,328	3,551	2,826	2,164	2,392	2,773
Total	**20,720**	**18,034**	**12,998**	**21,391**	**20,313**	**14,694**	**16,979**	**14,405**	**8,699**	**7,930**	**32,722**

Source: Ernst & Young 2011

Figure 4 US yearly biotechnology financing (US $m)

1.3.4 Life cycle of a biopharmaceutical company

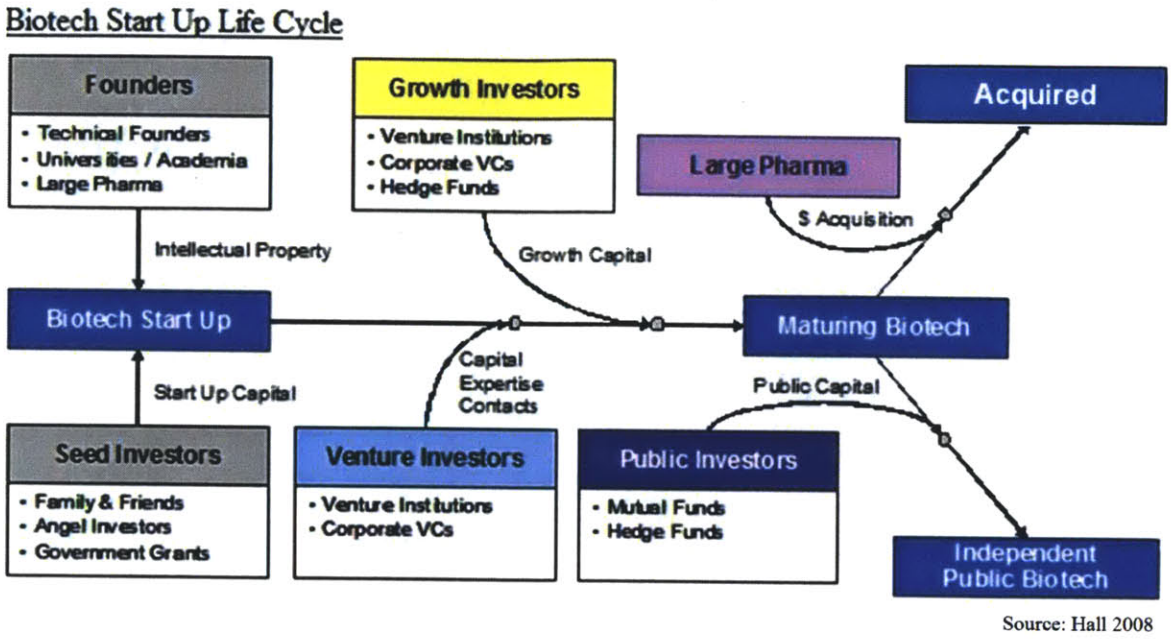
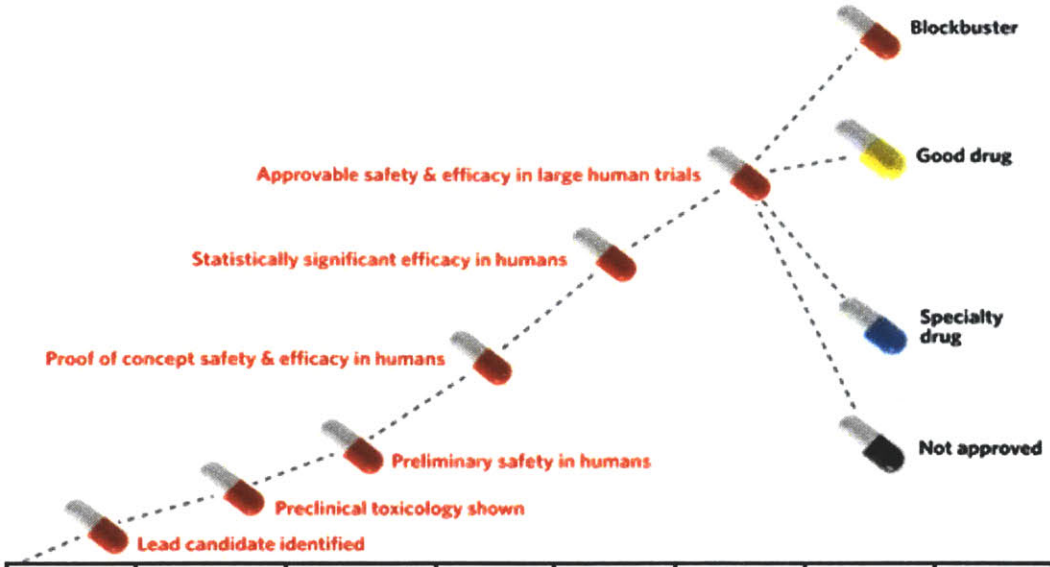


Figure 5 Lifecycle of biotech start up and its constituencies

Throughout the financial lifecycle of a biopharmaceutical start up, there are many stakeholders that get involved to help the company to reach the next value creating stage. Figure 5 provides an overview of different constituencies contributing at various points in the company's financial lifecycle from the seed stage to its maturity.



Phase	Discovery	Preclinical	Phase1	Phase 1b/2a	Phase 2b	Phase 3	FDA Review	Marketed Drug
Typical Cost ($mm)	$5	$5-10	$5-10	$10-15	$15-25	$40-100	$5	$100s
Sources of Capital	Seed Venture	Venture Seed	Venture Seed	Venture Growth	Venture Growth Public	Venture Growth Venture	Public Growth	Public

Source: Hall 2008

Figure 6 Financial life cycle of biopharmaceutical company

The initial funding or "seed capital" of a growing biotech company is typically made up of a number of sources such as government or institutional grants, family, friends, and wealthy individuals ("angel investors"). Such funding is relatively modest, typically less than $5 million. At this early stage, the founders, often the innovators and co-investors, own 100% of the company.

As the company successfully moves away from labs and animal studies and towards human clinical trials, its capital requirement grows significantly. To be able to test a compound in humans in the US, a number of in vitro and in vivo preclinical tests must be completed and then an investigational new drug (IND) application must be filed with the FDA. This process typically costs around $5-10 million for a single drug. At this juncture, the initial investors have a choice

whether to maintain their ownership share of the company and invest additional capital. Most of the time, the large capital requirement for IND-enabling studies goes beyond what typical angel investors are willing to invest and therefore, the company needs to seek new sources of financing.

This is where VC comes into a company's lifecycle. As mentioned in the earlier section, VC firms typically manage pools of money contributed from university endowments, pension funds, and other large institutions. They then seek promising early-stage companies in which they can invest. Given that typical venture capitalists prefer three to seven years to realize their returns, companies with realistic monetizable value inflection points will be able to raise money from VC.

Venture investors typically seek both a dilutive equity stake in the company and significant control over its operations and strategic direction via controlling through a company's board of directors. The ownership shares given to new venture capital investors in exchange for their capital will come from those of the founders. Consequently the founders' shares get diluted and they will now own smaller portions of the company. Over the course of multiple rounds of new capital leading to an IPO, the founders' stake will be diluted even further.

Upon filing an IND application and receiving an approval from the FDA, the company can begin its clinical studies in patients or normal volunteers. Receiving this initial approval is a transformative step for a small biotech company. The value of the compound is increased, thus driving up the value of the company. Conversely, the company's need for capital increases enormously because of the cost of performing human studies. This means that once again the biotech will need to raise money.

A typical clinical testing goes through three successive phases. In Phase I, a small group of usually healthy individuals (20-80) are tested to establish safe dosage and identify potential side effects. Phase II trials are larger (100-300) and are conducted with subjects who have the targeted disease or condition. They are designed to obtain evidence on safety and preliminary data on efficacy. The final pre-approval phase, Phase III trial, also known as pivotal trial, requires a large number of patients (1000-3000) and is designed to confirm the study drug's

effectiveness, monitor side effects and compare it to commonly used treatments. Once the company believes that it has enough safety and efficacy data, it will submit either a new drug application (NDA) or a biological license application (BLA) to the FDA for review and approval (Clinicaltrials.gov).

At this stage of the company's life cycle, there will be other types of investors that may become interested in providing capital. Such types of investments are called "crossover funds" and they tend to invest in both growing private and more mature public companies. In addition, established pharmaceutical companies with their venture capital arm become interested. These new rounds of capital to support more advanced clinical development are often known as "Series D" and "Series E" rounds and so-called "mezzanine capital." These investors have even shorter investment time horizons typically ranging from a few months to one or two years. The growth capital that later-stage venture and crossover investors provide is typically used towards generating additional clinical data to identify the therapeutic value of the drug (Hall and Wood 2008).

Clinical proof of concept is one of the most significant value-inflection points in the cycle of a drug's development and in order to complete studies to generate meaningful data, it will require a significant amount capital as discussed in Section 1.2.2. Therefore in order to continue its trajectory, it is essential for the company to consider innovative forms of financing its drug development.

It is typically only at maturity that any of the investors including those from seed stage to crossover fund stage have the opportunity to realize a return on their investment. Since the biotech business model is based on monetizing IP, a biotech company enters its maturity only after advancing through multiple value inflection points and reaching the stage where its investors can realize a gain from their investment. There are several exit options available for these investors and it depends largely on the appetite of prospective public equity investors through an IPO and of established pharmaceutical companies for potential acquisition.

The rest of the thesis is organized as follows. Chapter 2 will discuss the objective and methodology of the study and Chapter 3 will discuss the results from the data analysis and the implications of the study findings. Lastly, potential short falls and next steps will be discussed in Chapter 4 to conclude the thesis.

2. Thesis objective and methodology

2.1 Objective

We set out to investigate factors that executives at small to mid-sized biopharmaceutical companies should consider around the time of drug launch, a critical event that can directly impact a company's valuation.

2.2 Hypotheses

a. Companies that provide their own estimates perform better than those that do not provide guidance for estimated sales. Providing their own estimates allows the company to set modest estimates compared to those set by the analysts without the company management's guidance.
b. Companies that succeed in launching a drug make aggressive business development decisions and raise additional capital at the "right time." Companies that raise additional capital before drug launch perform better than those that do so after the launch.
c. A partnership with a larger company contributes to a successful drug launch.
d. Drugs for specialty markets or with an orphan indication perform better than those for primary care markets.

2.3 Methodology

2.3.1 Data collection

A list of new molecular entities (NMEs) and biologics license applications (BLAs) that were approved by the FDA from January 1, 2000 – December 31, 2009 was compiled from the FDA website. A total of 253 products were identified (Appendix A). A list of companies that owned the product at the time of approval was also compiled.

To be included in this analysis, companies that launched the drug had to meet two requirements:

- The firm had to be listed on some US. Exchange at the time of drug approval
- Its market capitalization had to be less than $ 20B at the time of approval

Fifty-one drugs met these initial criteria. We then identified the US. launch date for these selected drugs using EvaluatePharma and company press releases.

We classified drugs as specialty pharmaceuticals or primary care products by reviewing company press-releases for a specific designation and interviewing a physician to determine whether specialists or PCPs were the primary prescribers. We excluded 5 drugs that were non-therapeutic such as diagnostics or imaging agents.

Ultimately, the database for analysis included 46 drugs. The full list of drugs included in our study is provided in Appendix B.

We then collected data on several key variables we hypothesized to have correlation with change in stock price and/or market capitalization. To test Hypothesis (a), management sale guidance data was compiled by reviewing business updates and earnings conference call transcripts within one year before and after the launch date (Appendix C); Thomson ONE research database was used to access the reports. Historical analyst sales estimates were obtained from EvaluatePharma. Estimates that were made within one year before and one year after the launch were collected on a quarterly basis. At each date, I captured sales estimates for the launch year (Y=0) and that of years 1, 2 and 3 after the launch. The companies' actual sales data for the first two years after the launch date was also collected from EvaluatePharma database.

For Hypothesis (b), Capital IQ was used to capture public follow-on financing activities within a period of two years before and two years after the launch. The type of security and both file and offering dates were captured to calculate file-to-offer discounts.

Partnership information was collected from commercial databases including EvaluatePharma and Capital IQ to test Hypothesis (c). If there was a partnership at launch, the type of partnership

(e.g. co-promotion and/or co-development) was also captured. Company press releases were also used to cross check the information. Market related data including share price and market capitalization of the partnering company was obtained from Capital IQ and FactSet.

Lastly for hypothesis (d), primary drug indication was collected from EvaluatePharma. Company press releases were used to identify whether specialists or PCPs were the primary prescribers. The findings were confirmed with a primary care physician from Massachusetts General Hospital.

2.3.2 Data analysis

We benchmarked the performance of these companies across both stock price and market capitalization with the performance of the Nasdaq Biotechnology Index (NBI). We used market capitalization, in addition to stock price, to be sure we captured the impact of company stock issuances. To isolate the performance of each company from the background performance of the market, each company's change in stock price or market capitalization was adjusted for the underlying performance of the NBI during the relevant time period.

Because the launch of a product typically triggered a fluctuation of a company's market capitalization, we normalized company stock price and market capitalization to themselves at six months prior to drug launch. Since we adjusted each company's individual performance to the performance of the market, we were able to directly compare the performance of all companies between January 2000 and December 2009. We were also able to compare large and small companies, because we measured performance as a percent of stock price and market capitalization.

2.3.3 Regression modeling

Predictor variables that were initially considered in the analysis are the following: guidance (binary), partnership (binary), market size of the partner(s) at the time of launch, specialty/primary care indication (binary), difference between year two actual sales number and

that of pre-launch estimate, difference between year two actual sales number and that of post-launch estimate, financing activity prior to launch (binary), financing activity after launch (binary), average pre-launch file-to-offer discount, average post-launch file-to-offer discount, number of drugs launched by the same company (control variable) and NBI performance (control variable).

We then performed multiple linear regression analyses to determine which of these parameters were predictive of change in market value using the software package JMP9.

It is worth reemphasizing that the purpose of our model is to understand which variable is significant and how it will impact the average financial performance of the companies, not to make a precise prediction of the financial performance of the individual companies. A number of different combinations of variables were used to construct various models. Given the unavoidable multicollinearity, several combinations of variables are used to generate outputs from various models. It is possible to detect the sensitivity of a variable, i.e. how easily the parameter estimate changes upon adding or removing other variables. Therefore, the more sensitive the variable is, the more dependent it is on other variables in the model. Therefore such a variable is not informative as it provides inconsistent interpretation. Conversely, a variable that consistently demonstrates a significant relationship with minimal fluctuation in its impact on the overall model would be an informative variable; it could be used as an additional tool to aid the management when considering various factors during the time around a drug launch.

3. Results

3.1 Model 1: percentage change of stock price

Through multiple iterations, our analysis identified that three of the previously stated variables from Section 2.3.3 explain the change in stock price of the company: management guidance, actual sales beating analysts' estimates made post-launch date (actual sales at Year 2 since launch > analyst estimates made post-launch) and post-launch financing.

The primary driver is whether or not the management provides guidance. Guidance contributes significantly throughout different models, confirming our proposition that it is a solidly unique contributor to the change in share price. Giving guidance accounts for a 75% decline (estimate of 0.25) in share price from six months before the event to two years after the drug launch. Its impact in the model is very significant.

Secondly, beating analysts' sales estimates that were made post-launch also was consistently significant among different models. Drugs that beat analyst estimates made post-launch contributed to a 6% increase in stock price from six-months prior to the drug launch to two years after the launch.

Lastly, timing of financing was identified as another informative variable. Stocks of companies that raised additional capital after the drug launch performed better by 24% than those that pursued financing before the launch or did not pursue financing at all.

In addition to understanding which factors played a role in driving the performance of share price, it is equally important to understand the factors that were not significant. Having a partnership at launch does not contribute significantly to percent change in share price. That outcome might be indicating that managing expectations at the time of launch is more relevant. In addition, being a specialty/orphan drug does not correlate with change in share price. Its impact gets completely washed out (estimates close to zero) when other variables change in the

model. Having a partnership or being a specialty drug perhaps inherently bestows greater merits on the product but does not contribute to share performance.

3.2 Model 2: percentage change of market capitalization

Through multiple iterations, our analysis identified that two of the previously stated variables from Section 2.3.3 explain the change in market capitalization of the company: management guidance and post-launch financing.

Similar to what was observed in the share price performance analyses, whether or not the management provides guidance was the primary driver. Guidance contributes significantly throughout different models, confirming our belief that it is a solidly unique contributor to the change in market capitalization. Giving guidance accounts for a 45% decline in the market capitalization from six months before to two years after the drug launch.

Timing of financing was also consistently significant throughout the analyses. The companies that raised additional capital after the drug launch experienced a 28% larger change in the market capitalization than those that raised capital before the launch or did not pursue financing at all.

Variables that were not significant in the model can equally be informative and are worth the effort to understand the potential implications of the findings. Neither having a partnership nor being a specialty drug contributes significantly to changes in market capitalization of the company around the time of a drug launch.

4. Discussion

Hypothesis (a) was based on an assumption that managements who offer guidance are more conservative in projecting their future sales in the hopes of guiding the Street to publish more tangible sales goals for the company. The results from our study suggest otherwise. Two years after the drug launch, shares of companies that provided guidance around the time of a drug launch were down from the prices at six months before the launch. A similar relationship was observed when the model looked at the changes in the market capitalization. A potential interpretation of the result could be that those companies that provide guidance may have greater confidence in the performance of the drug in the market and unintentionally portray a rosier future. Setting the expectation higher may have led the market to be disappointed with the actual performance of the drug in the market, which consequently punished the company's stock.

The regression outcome for the impact of analyst estimates and actual sales data was not surprising. One would rightly expect that analyst estimates will get refined as time progresses and the uncertainty associated with launch decreases. Based on this reasoning, it is reasonable that the investment community puts greater emphasis on how the company performs against the analysts' estimates made on a later date.

With such a high degree of uncertainty associated with drug launches, shorting against the launch now has become a widespread investment strategy. With this pattern in the industry, hypothesis (b) was based on an assumption that the public would be generally disappointed with the drug's performance after the launch. Therefore raising additional capital post-drug launch would be less favorable to the company's financial performance compared to pursuing additional financing before the launch. Interestingly enough, the timing of financing was significant amongst various models, yet the outcome was contrary to our expectation. Companies that pursued additional rounds of financing after the drug launch performed better both from the stock price performance perspective and that of the market capitalization. There are many possible explanations for this observation. One might be that companies with more positive outlooks on their drug performance may have pursued additional rounds of financing and indeed

were able to secure more funding to conduct post-commercialization activities that led to a successful performance.

Another potential interpretation of this observation may come from a mechanical aspect of financing in general. If a company pursues an additional round of financing before the launch, the impact of an earlier dilution might be greater and might linger for a longer period of time. Such a dilution effect could be reflected in the stock performance of those companies that raised additional financing before the drug launch.

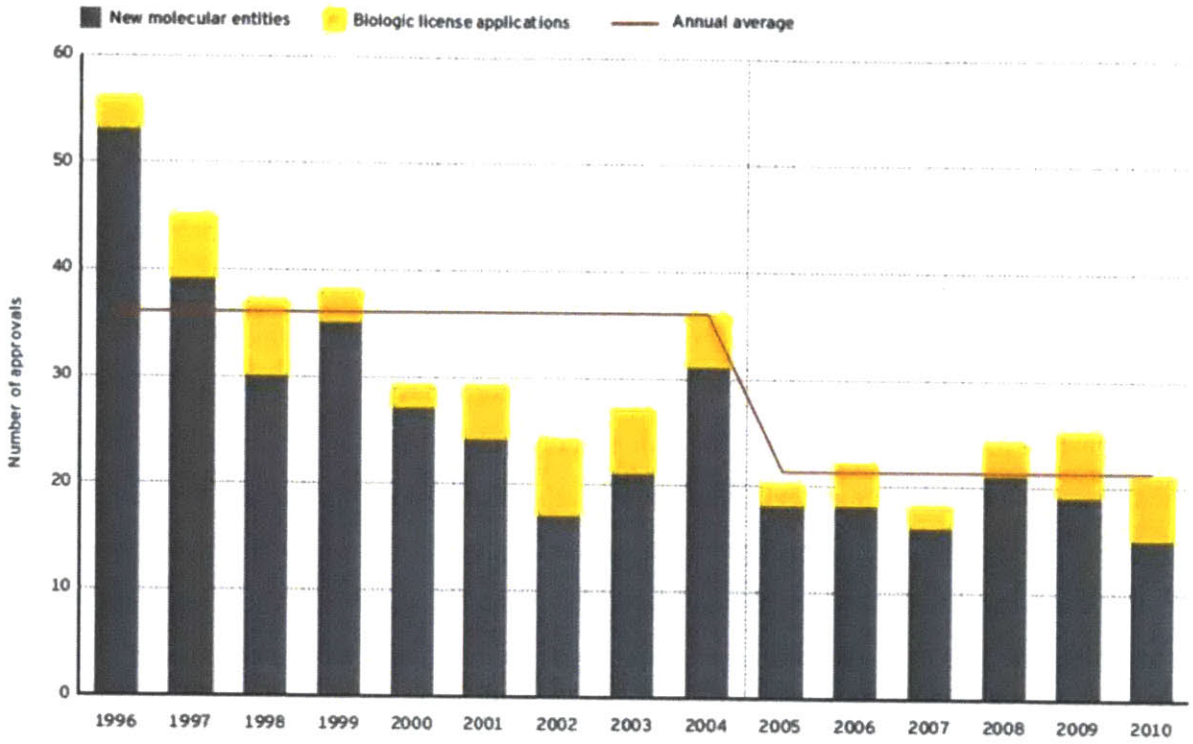
Neither a partnership nor the market size of the partner contributed to either of the outcome measures. Whether or not the product is a specialty product also did not make any significant contribution to the models. These findings were particularly striking. Hypothesis (c) assumed that having a partner, especially if the partner was larger than the company launching the drug, might contribute to the success of a drug launch due to the partnering company's resources. With the recent commercial success of specialty pharmaceuticals as described by Gudiksen et al. (2008), our hypothesis (d) was set out to test whether a specialty drug's novel concept would translate to a better performance of the stock. Our finding does not necessarily contradict the findings of previous studies, but rather suggests that the performance of stock and/or market capitalization is largely driven by managing the expectation of the investors rather than more intrinsic attributes of the product. The market may have already priced in good performance of those drugs and did not reward their performance, as it was already expected

5. Conclusion

This study was not designed to provide a prescriptive answer to what will lead to a successful drug launch. The findings from this study, however, will provide several valuable advising tools for management during the period around a drug launch. Bringing a product to market is a critical event for any biopharmaceutical company. It marks a major turning point within the biopharmaceutical's lifecycle and the company that can successfully launch a product will be viewed as a different asset class, one that has a lower risk profile. Therefore, it is critical to understand potential drivers of the value and to encourage executives to raise provocative questions when they are pursuing the next round of financing or whether to provide guidance. This study suggests that there are several possible strategic and actionable considerations that can guide management to ask the right questions. Asking the right questions will help management make better decisions that will eventually translate to a better stock performance and possibly a growth in market capitalization in the course of a drug launch. We found that those companies that did not provide guidance at the time of launch and raised additional capital within two years after launch performed better than that did otherwise. There are many other strategic principles, such as building a sustainable pipeline, which a company should consider to become an enduring player in this rapidly changing industry.

There are several limitations to the study. Firstly, this study was based on a small sample size. Nonetheless, ascertainment of a larger study data set is unachievable in that there are only a certain number of drugs produced by small- to mid-cap companies that receive FDA approval. In addition, some of the historical data, such as analyst estimates of sales or management's sales guidance, are inherently challenging to retrieve. Given that the sample of 46 was small and that this research was not a designed study, we did not use R-square value. We believe, however, that for our study purposes, the small sample size does not pose major problems for our analysis because this study was not intended to provide quantitative prediction but to provide a list of factors that management would do well to consider during the period around a drug launch.

Appendices



Appendix A FDA product approvals 1996-2010

(Sources: Ernst & Young 2011)

Drug Name	Company	Date of Approval	Market Capitalization at Approval ($ millions)	Date of Launch	Market Capitalization at Launch ($ millions)	Specialty (1) vs. Primary care (0)
IPLEX	INSMED Incorp					
HYLENEX RECOMBINANT	HALOZYME THERAP					
BEPREVE	ISTA PHARMS					
ENTEREG	ADOLOR					
VITRASE	ISTA PHARMS					
REMODULIN	UNITED THERAP					
INCRELEX	TERCICA					
RELISTOR	PROGENICS					
KALBITOR	DYAX CORP.					
CUBICIN	CUBIST					
NAGLAZYME	BIOMARIN					
FOLOTYN	ALLOS					
ANGIOMAX	MEDICINES CO					
XIFAXAN	SALIX PHARMS					
NATRECOR	SCIOS					
VIBATIV	THERAVANCE INC					
CLEVIPREX	MEDICINES CO					
SOLIRIS	ALEXION PHARM					
ARCALYST	REGENERON PHARMACEUTICALS					
BYETTA	AMYLIN					
TRISENOX	CELL THERAPEUTICS					
SYMLIN	AMYLIN					
ERBITUX	IMCLONE					
RAPAFLO	WATSON LABS					
KUVAN	BIOMARIN PHARM					
TARCEVA	OSI PHARMS					
VELCADE	MILLENNIUM PHARMS					
TREANDA	CEPHALON					
VIDAZA	PHARMION					
TRELSTAR	WATSON LABS					
LUNESTA	SUNOVION PHARMS INC (FORMER SUPRACOR, SEPR)					
VIREAD	GILEAD					
HEPSERA	GILEAD					
LUMIGAN	ALLERGAN					
REVLIMID	CELGENE					
ELESTAT	ALLERGAN					
EMTRIVA	GILEAD					
BYSTOLIC	FOREST LABS					
CLOLAR	GENZYME					
MYOZYME	GENZYME					
MOZOBIL	GENZYME					
NAMENDA	FOREST LABS					
CAMPRAL	FOREST LABS					
TYSABRI	BIOGEN IDEC					
COLAZAL	SALIX PHARMS					
CAMPATH	ILEX PHARMACEUTICALS					

Appendix B List of drugs and companies analyzed

(Sources: FDA website, EvaluatePharma, Capital IQ, Thomson One research reports, company press-releases and interviews with a physician)

Appendix C Selected Commentary for Management Guidance

- *"Baxter expects sales of HYLENEX, including co-formulations as well as kitted products, could potentially reach $500 million."* –Baxter International Investor Day, Brean Murray Carret & Co. Analyst Report 3/15/07
- *"We expect 2008 net sales of Kuvan to be in the range of $35 million to $70 million. This wide range is attributable to the many uncertainties with first year product launches and also variables that take into consideration the average patient weight and dose, the logistics of getting patients tested in the clinics and patient compliance."* –Biomarine Pharmaceutical conference call 12/13/07
- *"We deferred revenue on these orders in the third quarter as Cleviprex is a new product and we do not have enough history to estimate our gross to net adjustments or sales patterns. However, we reiterate our full-year 2008 guidance for Cleviprex of $5 million to $10 million."*- Medicines Company conference call 10/22/08

		Outputs		Controls		
Drug Name	Company	Share price 2- yrs post/6-mo prior	Mkt cap 2-yr post/Mkt cap 6-mo prior launch	# of drugs launched by the same company	NBI performance (2yr post/6mo prior)	# of days bt approval and launch
IPLEX	INSMED Incorp					
HYLENEX RECOMBINANT	HALOZYME THERAP					
BEPREVE	ISTA PHARMS					
ENTEREG	ADOLOR					
VITRASE	ISTA PHARMS					
REMODULIN	UNITED THERAP					
INCRELEX	TERCICA					
RELISTOR	PROGENICS					
KALBITOR	DYAX CORP.					
CUBICIN	CUBIST					
NAGLAZYME	BIOMARIN					
FOLOTYN	ALLOS					
ANGIOMAX	MEDICINES CO					
XIFAXAN	SALIX PHARMS					
NATRECOR	SCIOS					
VIBATIV	THERAVANCE INC					
CLEVIPREX	MEDICINES CO					
SOLIRIS	ALEXION PHARM					
ARCALYST	REGENERON PHARMACEUTICALS					
BYETTA	AMYLIN					
TRISENOX	Cell Therapeutics (CTIC)					
SYMLIN	AMYLIN					
ERBITUX	IMCLONE					
RAPAFLO	WATSON LABS					
KUVAN	BIOMARIN PHARM					
TARCEVA	OSI PHARMS					
VELCADE	MILLENNIUM PHARMS					
TREANDA	CEPHALON					
VIDAZA	Pharmion					
TRELSTAR	WATSON LABS					
	SUNOVION PHARMS INC (former					
LUNESTA	Supracor, SEPR, until 10/12/10)					
VIREAD	GILEAD					
HEPSERA	GILEAD					
LUMIGAN	ALLERGAN					
REVLIMID	CELGENE					
ELESTAT	ALLERGAN					
EMTRIVA	GILEAD					
BYSTOLIC	FOREST LABS					
CLOLAR	GENZYME					
MYOZYME	GENZYME					
MOZOBIL	GENZYME					
NAMENDA	FOREST LABS					
CAMPRAL	FOREST LABS					
TYSABRI	BIOGEN IDEC					
COLAZAL	SALIX PHARMS					
CAMPATH	ILEX PHARMACEUTICALS					

Appendix D Regression output and control variables

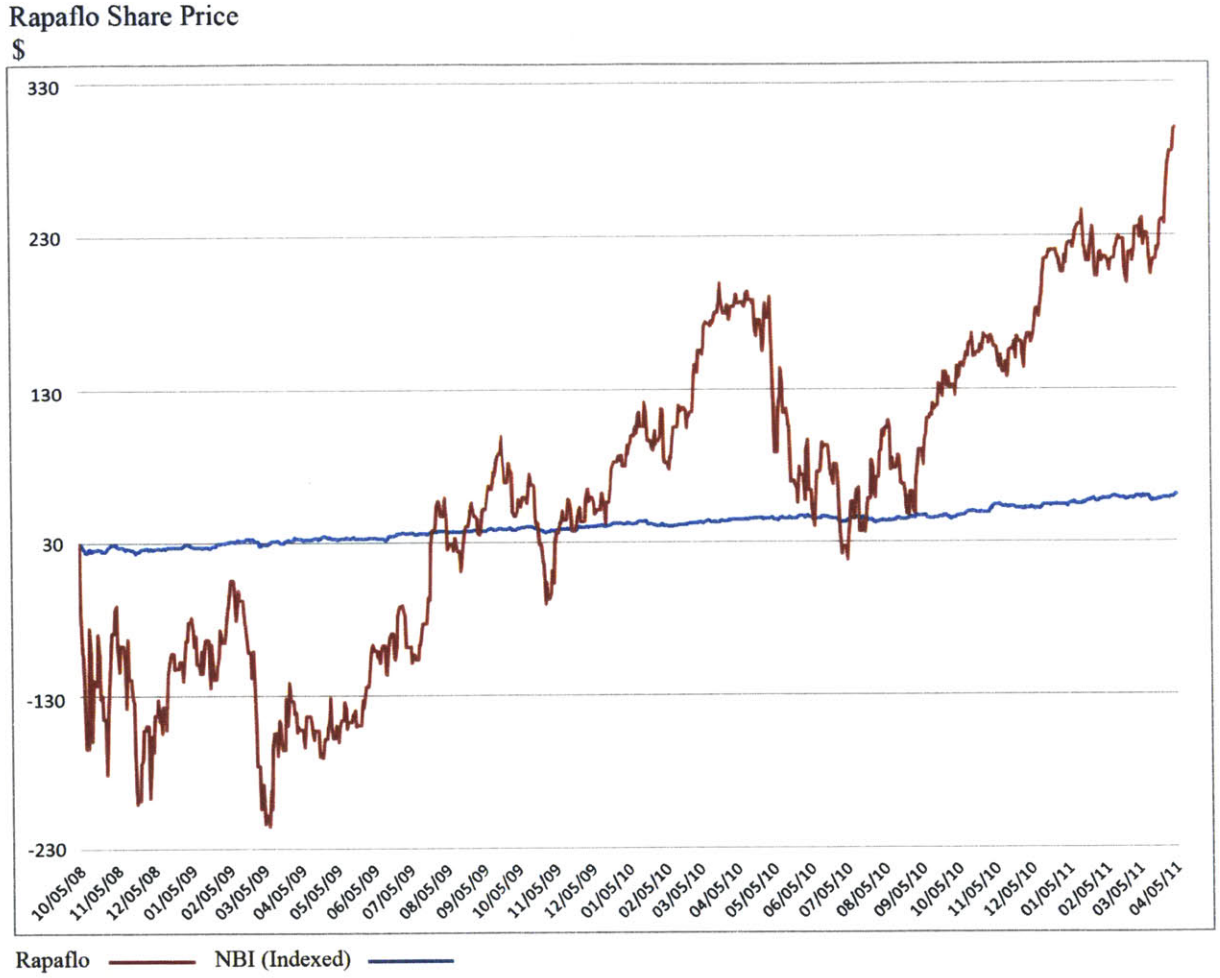
(Sources: FDA website, EvaluatePharma, Capital IQ, Thomson One research reports, company press-releases and interviews with a physician)

Appendix E (Continues) Regression predictor variables

		Variables											
Drug Name	Company	Guidance (Y=1, N=0)	Partnership (Y=1, N=0)	Total Mkt cap of partner(s)	Orphan indication (Y=1, N=0)	Diff (2-yr actual vs pre-launch estimate)	Diff (2-yr actual vs post-launch estimate)	Actual sales > pre-launch estimate (Y=1, N=0)	Actual sales > post-launch estimate (Y=1, N=0)	Pre-launch financing (Y=1, N=0)	Post-launch financing (Y=1, N=0)	Pre-launch FTO discount	Post-launch FTO discount
IFLEX	INSMED Incorp												
HYLENEX RECOMBINANT	HALOZYME THERAP												
BEPREVE	ISTA PHARMS												
ENTEREG	ADOLOR												
VITRASE	ISTA PHARMS												
REMODULIN	UNITED THERAP												
INCRELEX	TEROCA												
RELISTOR	PROGENICS												
KALBITOR	DYAX CORP.												
CUBICIN	CUBIST												
NAGLAZYME	BIOMARIN												
FOLOTYN	ALLOS												
ANGIOMAX	MEDICINES CO												
XIFAXAN	SALIX PHARMS												
NATRECOR	SCIOS												
VIBATIV	THERAVANCE INC												
CLEVIPREX	MEDICINES CO												
SOLIRIS	ALEXION PHARM												
ARCALYST	REGENERON PHARMACEUTICALS												
BYETTA	AMYLIN												
TRISENOX	Cell Therapeutics (CTIC)												
SYMLIN	AMYLIN												
ERBITUX	IMCLONE												
RAPAFLO	WATSON LABS												
KUVAN	BIOMARIN PHARM												
TARCEVA	OSI PHARMS												
VELCADE	MILLENNIUM PHARMS												
TREANDA	CEPHALON												
VIDAZA	Pharmion												
TRELSTAR	WATSON LABS												
LUNESTA	SUNOVION PHARMS INC (former Sepracor, SEPR, until 10/12/10)												
VIREAD	GILEAD												
HEPSERA	GILEAD												
LUMIGAN	ALLERGAN												
REVLIMID	CELGENE												
ELESTAT	ALLERGAN												
EMTRIVA	GILEAD												
BYSTOLIC	FOREST LABS												
CLOLAR	GENZYME												
MYOZYME	GENZYME												
MOZOBIL	GENZYME												
NAMENDA	FOREST LABS												
CAMPRAL	FOREST LABS												
TYSABRI	BIOGEN IDEC												
COLAZAL	SALIX PHARMS												
CAMPATH	ILEX PHARMACEUTICALS												

Relative Share Price Performance

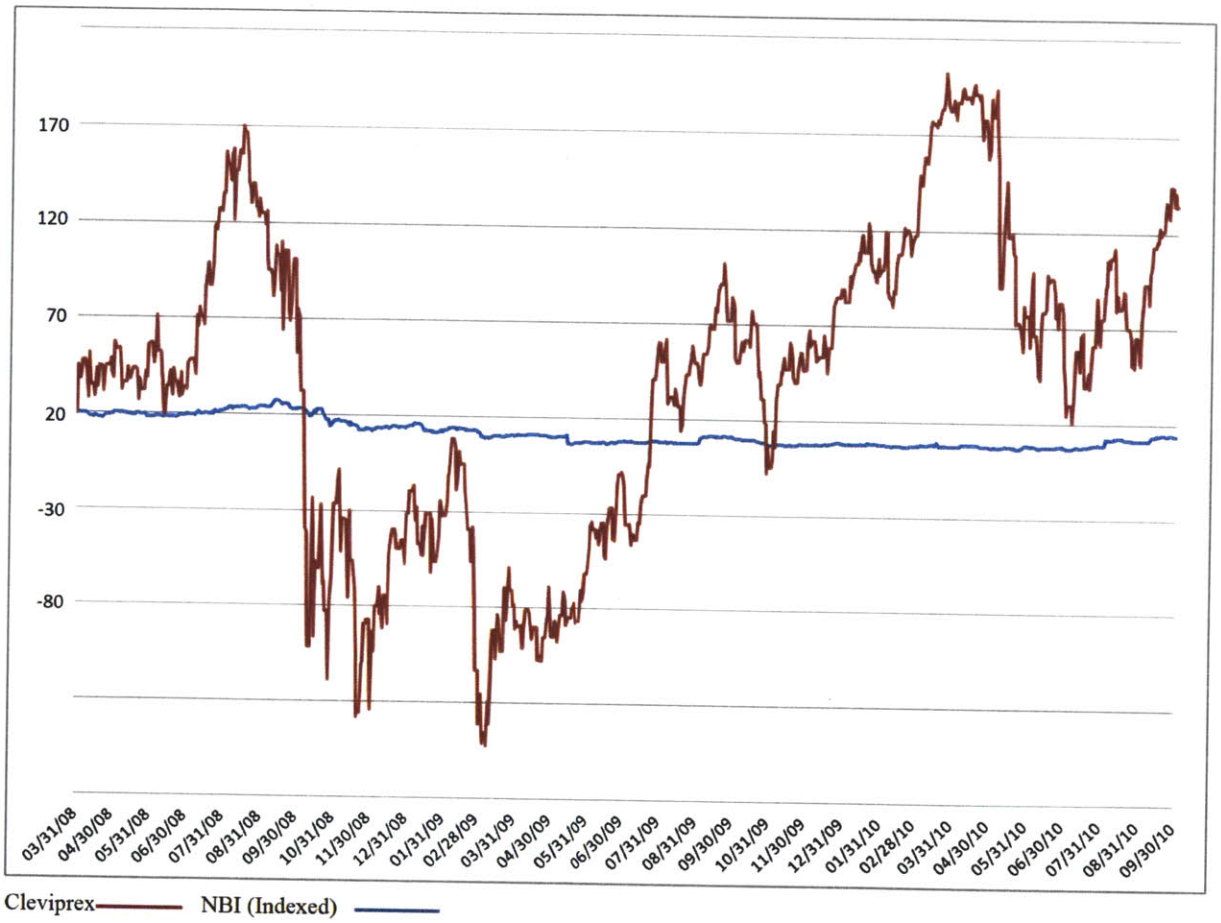
Since Six Month Pre- to Two Years Post-Launch



Appendix F Relative share price performance: Rapaflo

Relative Share Price Performance

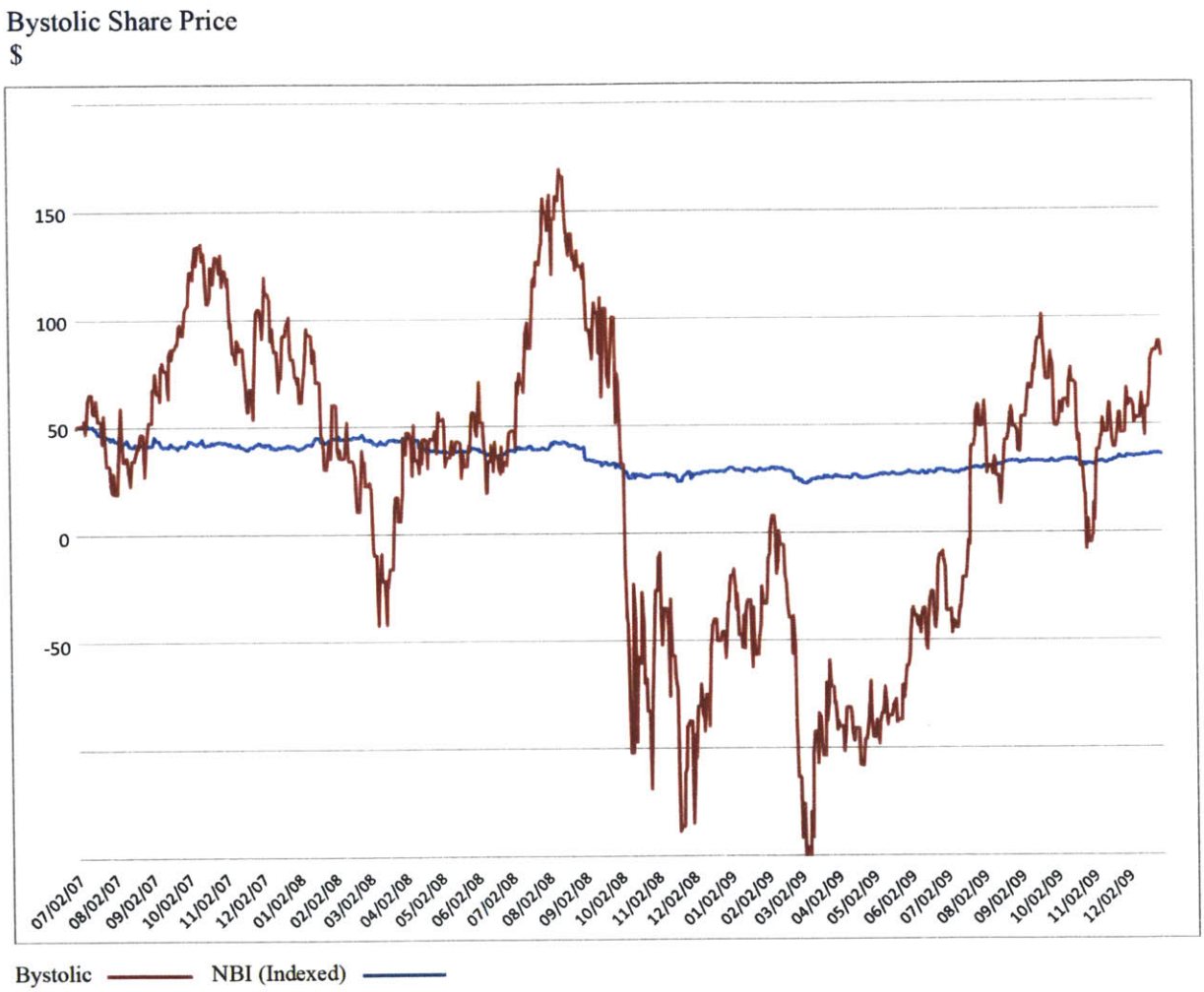
Since Six Month Pre- to Two Years Post-Launch



Appendix G Relative share price performance: Cleviprex

Relative Share Price Performance

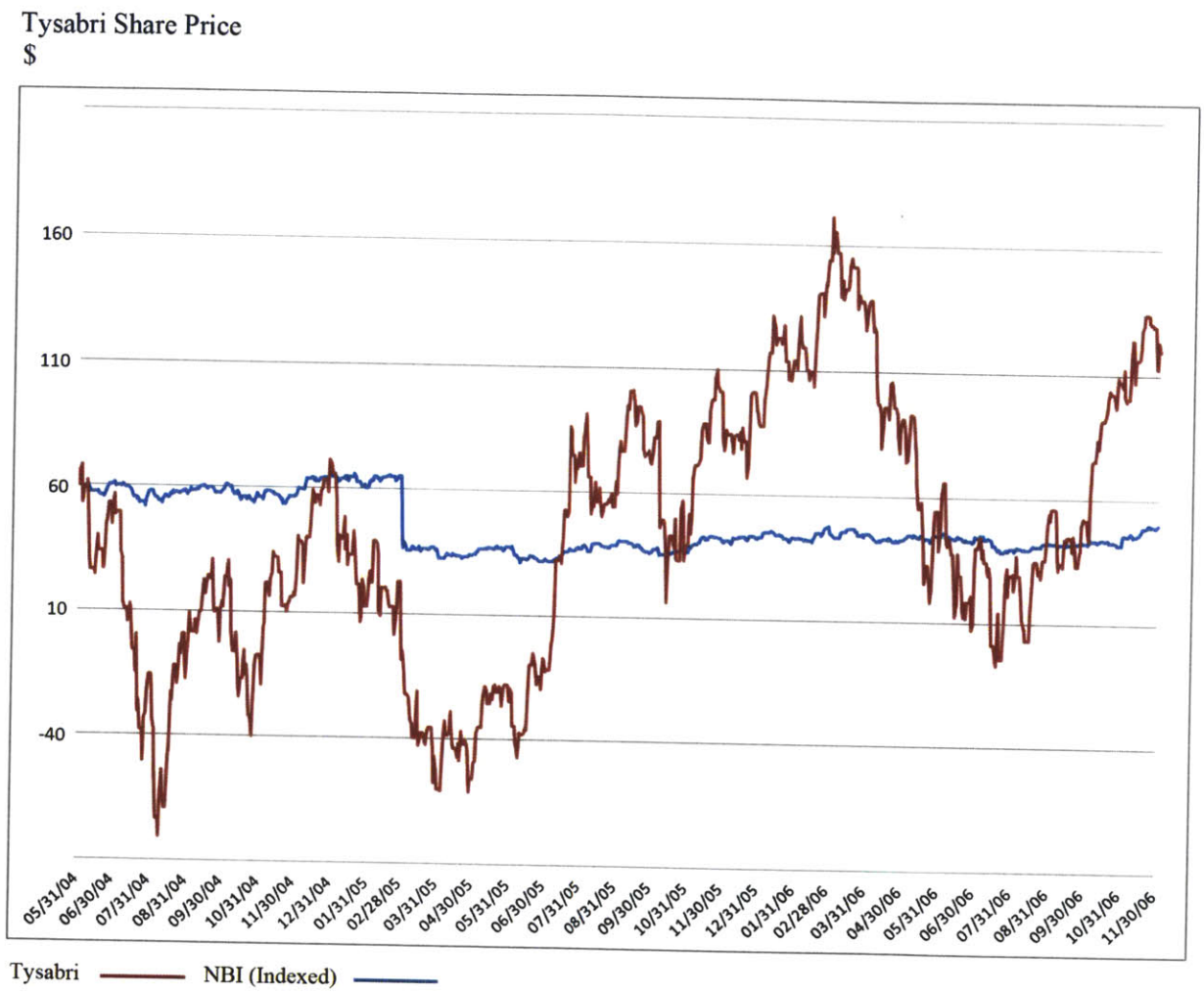
Since Six Month Pre- to Two Years Post-Launch



Appendix H Relative share price performance: Bystolic

Relative Share Price Performance

Since Six Month Pre- to Two Years Post-Launch



Appendix I Relative share price performance: Tysabri

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